



4164-01-P

## **DEPARTMENT OF HEALTH AND HUMAN SERVICES**

### **Food and Drug Administration**

**[Docket No. FDA-2010-N-0117]**

**Agency Information Collection Activities; Proposed Collection; Comment Request;**

### **Guidance for Industry on Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA or Agency) is announcing an opportunity for public comment on the proposed collection of certain information by the Agency. Under the Paperwork Reduction Act of 1995 (PRA), Federal Agencies are required to publish notice in the *Federal Register* concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on the information collection associated with the FDA “Guidance for Industry on Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims,” which is intended to assist applicants in developing labeling for outcome claims for drugs that are indicated to treat hypertension.

**DATES:** Submit either electronic or written comments on the collection of information by

**[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*].**

**ADDRESSES:** You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before

**[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**. The <https://www.regulations.gov> electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of **[INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]**. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are postmarked or the delivery service acceptance receipt is on or before that date.

#### *Electronic Submissions*

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <https://www.regulations.gov>. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to <https://www.regulations.gov> will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on <https://www.regulations.gov>.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

#### *Written/Paper Submissions*

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in “Instructions.”

*Instructions:* All submissions received must include the Docket No. FDA-2010-N-0117 for “Agency Information Collection Activities; Proposed Collection; Comment Request; Guidance for Industry on Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims.” Received comments, those filed in a timely manner (see ADDRESSES), will be placed in the docket and, except for those submitted as “Confidential Submissions,” publicly viewable at <https://www.regulations.gov> or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states “THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.” The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on <https://www.regulations.gov>. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover

sheet and not in the body of your comments and you must identify this information as “confidential.” Any information marked as “confidential” will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA’s posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: <https://www.gpo.gov/fdsys/pkg/FR-2015-09-18/pdf/2015-23389.pdf>.

*Docket:* For access to the docket to read background documents or the electronic and written/paper comments received, go to <https://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Domini Bean, Office of Operations, Food and Drug Administration, Three White Flint North, 10A-12M, 11601 Landsdown St., North Bethesda, MD 20852, 301-796-5733, [PRASStaff@fda.hhs.gov](mailto:PRASStaff@fda.hhs.gov).

**SUPPLEMENTARY INFORMATION:** Under the PRA (44 U.S.C. 3501-3520), Federal Agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. “Collection of information” is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes Agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal Agencies to provide a 60-day notice in the *Federal Register* concerning each proposed collection of information, including each proposed extension of an existing collection of information, before

submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Guidance for Industry on Hypertension Indication: Drug Labeling For Cardiovascular Outcome

Claims

OMB Control Number 0910-0670--Extension

This information collection request supports recommendations found in Agency guidance. The document entitled, "Guidance for Industry; Hypertension Indication: Drug Labeling for Cardiovascular Outcome Claims," available from our website at <https://www.fda.gov/media/71824/download>, encourages the submission of supplemental labeling and is intended to assist applicants in developing labeling for outcome claims for drugs that are indicated to treat hypertension, and to provide common labeling for antihypertensive drugs except where differences are clearly supported by clinical data.

With few exceptions, current labeling for antihypertensive drugs includes only the information that these drugs are indicated to reduce blood pressure; the labeling does not include information on the clinical benefits related to cardiovascular outcomes expected from such blood

pressure reduction. However, blood pressure control is well established as beneficial in preventing serious cardiovascular events, and inadequate treatment of hypertension is acknowledged as a significant public health problem. We believe that the appropriate use of these drugs can be encouraged by making the connection between lower blood pressure and improved cardiovascular outcomes more explicit in labeling.

As discussed in the guidance, we therefore recommend the following information collection:

1. Section IV.C of the guidance requests that the CLINICAL STUDIES section of the Full Prescribing Information of the labeling should include a summary of placebo or active-controlled trials showing evidence of the specific drug's effectiveness in lowering blood pressure. If trials demonstrating cardiovascular outcome benefits exist, those trials also should be summarized in this section. Table 1 in section V of the guidance contains the specific drugs for which FDA has concluded that such trials exist. If there are no cardiovascular outcome data to cite, one of the following two paragraphs should appear:

- “There are no trials of [DRUGNAME] or members of the [name of pharmacologic class] pharmacologic class demonstrating reductions in cardiovascular risk in patients with hypertension,” or
- “There are no trials of [DRUGNAME] demonstrating reductions in cardiovascular risk in patients with hypertension, but at least one pharmacologically similar drug has demonstrated such benefits.”

In the latter case, the applicant's submission generally should refer to table 1 in section V of the guidance. If the applicant believes that table 1 is incomplete, it should submit the clinical evidence for the additional information to Docket No. FDA-2008-D-0150. The

labeling submission should reference the submission to the docket. We estimate that no more than one submission to the docket will be made annually from one company, and that each submission will take approximately 10 hours to prepare and submit. Recommendations for the CLINICAL STUDIES section of the Full Prescribing Information of the labeling are covered by FDA regulations at §§ 201.56 and 201.57 (21 CFR 201.56 and 201.57) and require such labeling. The information collection associated with these regulations is approved under OMB control number 0910-0572.

2. Section VI.B of the guidance requests that the format of the cardiovascular outcome claim submitted to FDA in a prior approval supplement include the following information:

- A statement that the submission is a cardiovascular outcome claim supplement, with reference to the guidance and related Docket No. FDA-2008-D-0150
- Applicable FDA forms (e.g., 356h, 3397)
- Detailed table of contents
- Revised labeling to include:
  - Draft revised labeling conforming to the requirements in §§ 201.56 and 201.57, and
  - Marked-up copy of the latest approved labeling, showing all additions and deletions, with annotations of where supporting data (if applicable) are located in the submission.

We estimate that on average, 4 cardiovascular outcome claim supplements will be submitted annually from 4 different companies, and that each supplement will take approximately 20 hours to prepare and submit. The guidance also recommends that other labeling changes (e.g., the addition of adverse event data) should be minimized and provided in

separate supplements, and that the revision of labeling to conform to §§ 201.56 and 201.57 may require substantial revision to the ADVERSE REACTIONS or other labeling sections.

3. Section VI.C of the guidance states that applicants are encouraged to include the following statement in the drug's promotional materials:

- “[DRUGNAME] reduces blood pressure, which reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. Controlling high blood pressure should be part of comprehensive cardiovascular risk management, including, as appropriate, lipid control, diabetes management, antithrombotic therapy, smoking cessation, exercise, and limited sodium intake. Many patients will require more than one drug to achieve blood pressure goals.”

The inclusion of this statement in the promotional materials for the drug is exempt from OMB review under 5 CFR 1320.3(c)(2).

We estimate the burden of the information collection as follows:

Table 1.--Estimated Annual Reporting Burden<sup>1</sup>

| Activity                                           | No. of Respondents | No. of Responses per Respondent | Total Annual Responses | Hours per Response | Total Hours |
|----------------------------------------------------|--------------------|---------------------------------|------------------------|--------------------|-------------|
| Submission to Docket No. FDA-2008-D-0150           | 1                  | 1                               | 1                      | 10                 | 10          |
| Cardiovascular Outcome Claim Supplement Submission | 4                  | 1                               | 4                      | 20                 | 80          |
| Total                                              |                    |                                 |                        |                    | 90          |

<sup>1</sup> There are no capital costs or operating and maintenance costs associated with this collection of information.

Our estimate for the information collection reflects an overall increase of burden. This increase corresponds to an increase in submissions we have received over the last few years.

Dated: July 9, 2019.

**Lowell J. Schiller,**

*Principal Associate Commissioner for Policy.*

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